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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,685	05/27/2005	Allan Otto Fog Lihme	036179-0111	9774

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,685	LIHME ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,6-12,15-17 and 19-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,6-12,15-17 and 19-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1, 3-5, 13-14, 18 and 28 are canceled. Claims 2, 6-12, 15-17 and 19-27 are under consideration in this office action.

Withdrawal of Objections

2. The objection of claim 18 under 37 CFR 1.75(c) is withdrawn in view of applicants' amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 2, 6-8, 11-12, 15-17, 19-21 and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman et al., (US Patent 6,090,292 published July 18, 2000) in view of Flickinger (US Patent 6,036,861 published March 14, 2000).

The rejection is on the grounds that it would have been prima facie obvious at the time of applicants invention to modify the extracorporeal adsorption method using fluidized bed adsorption as taught by Zimmerman et al., where the modification incorporates the particles having a density of at least 1.3 g/ml, a diameter in a range of 5-1000um and where the sedimented volume is at most 80% as taught Flickinger et al.,

in order to provide a significantly high and surprisingly substantially consistent dynamic protein binding capacity when expanded at high fluid velocity that also rapidly adsorb proteins.

Response to Arguments

4. Applicant's arguments filed June 14, 2010 have been fully considered but they are not persuasive.

The rejection of claims 2, 6-8, 11-12, 15-17, 19-21 and 24-27 under 35 U.S.C. 103(a) as being unpatentable over Zimmerman et al., in view of Flickinger is maintained for reasons already of record.

Applicants urge that the specification specifically describes what is meant by a "fluidized bed" and this description distinguishes packed bed columns, such as those described by Zimmerman, from fluidized beds, therefore Zimmerman does not describe a flow rate such that a fluidized bed of the particles is formed as recited by claim 2. First, applicants omit the statement within the specification which says

> "A 'fluidised bed" is herein defined as any arrangement of agitation, buffers and adsorbent particles in which a space between the individual particles wider than the minimum space obtained in a packed column of said particles is achieved. Thus, accordingly to this definition, any set of particles that are utilized in any type of non-packed bed reactor constitutes a 'fluidised bed'."

Contrary to applicants statement, the adsorption column assembly adapted for fluidized bed adsorption is met by the teachings of Zimmerman et al. Zimmerman et al., teach a method that treats blood by passing the blood through the adsorption column assembly at such a blood perfuses through the column in the direction such that toxin-bound or

albumin-bound toxin flows over the coated surface of the bead. Zimmerman et al., teach the method using an adsorption column assembly, comprising a column and an adsorption medium in the form of particles. Zimmerman et al., teach the sedimented volume of said particles being at the most 80% of the volume of the column. Zimmerman et al., teach the flow-through being collected at section 1,2 entitled Adsorption of Endotoxins From Human Plasma By Albumin-Coated Acrylic Resin Beads. Therefore applicants' argument drawn to the fluidized bed and flow rate is not persuasive.

Applicants assert that one of skill in the art would not expect Zimmerman's column to allow blood to pass through and exit the column with negative consequences. Contrary to applicants' assertion, Zimmerman et al., repeatedly teach a column allowing blood to flow through. Zimmerman et al., teach the method of treating blood by passing the blood through the adsorption column assembly (col. 2, lines 28-30). Zimmerman et al., teach the flow rate of the blood through the column assembly is such that expansion ratio of the fluidized bed is at least 1.3 (col. 4, lines 65-68). Section 1.2 entitled Experimental Procedure discloses whole blood from donors being passed over the packed columns (col. 6, lines 18-33). Claim 10 recites that solutions are selected from whole blood or plasma(see also col. 2, lines 25-29; col. 2, lines 65-68). Therefore applicants' assertion that one of skill in the art would expect Zimmerman's column to gradually clog and show serious decrease in functionality in the time required for adequate removal of the harmful substances is not persuasive since Zimmerman et al., clearly teach the use of adsorption column for passing blood, whole blood and plasma.

Applicants argue that Flickinger does not disclose extracorporeal adsorption for removing harmful substances responsible of inducing sepsis caused by Gram-negative or Gram-positive bacteria, as claimed. In response to applicant's arguments against the Flickinger reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, Zimmerman et al., clearly teach an extracorporeal adsorption method for removing harmful substances caused by Gram-negative or Gram-positive bacteria in a mammal. Therefore, this argument is not persuasive since the references used within the instant rejections, teach extracorporeal adsorption for removing harmful substances responsible of inducing sepsis caused by Gram-negative or Gram-positive bacteria.

Applicants urge that one of skill in the art would not necessarily expect that the types of adsorption columns would be interchangeable due to the very different properties of the columns and that Flickinger and Zimmerman do not teach or suggest the claimed method. In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.

1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, there is a reasonable expectation of success in incorporating the methods of Zimmerman et al., and Flinkinger et al., since both teach providing fluidized bed assemblies for removing substances using an adsorption column with particles having a density of at least 1.3 g/ml and having affinity specific molecules attached thereto with no change in the respective functions of the particles or the column, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. The claim would have been obvious because the substitution of known elements such as particles having a density of at least 1.3 g/ml and a mean diameter in the range of 5-1000 for another would have yielded predictable results which no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, this argument is not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2, 6-7, 9-10, 16-17, 20-23 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jaber et al., (American Journal of Kidney Diseases. Vol. 30,

No 5, Suppl. 4 (November), 1997: pages S44-S56) in view of Flinkinger et al (US Patent 6,036,861 published March 14, 2000).

Therefore the rejection is on the grounds that it would have been prima facie obvious at the time of applicants invention to modify the extracorporeal adsorption method using fluidized bed adsorption as taught by Jaber et al., where the modification incorporates the high density particles having a density of at least 1.3 g/ml, a diameter in a range of 5-1000um and where the sedimented volume is at most 80% as taught Flickinger et al., in order to provide a significantly high and surprisingly substantially consistent dynamic protein binding capacity when expanded at high fluid velocity that also rapidly adsorb proteins without the problems associated with Sepharose beads.

Response to Arguments

6. Applicant's arguments filed June 14, 2010 have been fully considered but they are not persuasive.

The rejection of claims 2, 6-7, 9-10, 16-17, 20-23 and 26-27 under 35 U.S.C. 103(a) as being unpatentable over Jaber et al., in view of Flickinger is maintained for reasons already of record.

Applicants urge that Jaber et al., fail to disclose the use of fluidized bed adsorption columns, as recited by the claims. However, applicant is reminded that a 'fluidised bed" is herein defined as any arrangement of agitation, buffers and adsorbent particles in which a space between the individual particles wider than the minimum

space obtained in a packed column of said particles is achieved. Thus, accordingly to this definition, any set of particles that are utilized in any type of non-packed bed reactor constitutes a 'fluidised bed'." Jaber et al., teach adsorbent-based blood purification founded upon adsorption, which removes harmful molecules by binding those molecules onto the surface of a material. Jaber et al., teach specific affinity molecules being antibodies coated onto micro spheres. Jaber et al., teach a flow rate of 200ml/min and hemoperfusion methods wherein the flow rate was 80-100ml/min. Therefore applicants' argument drawn to the fluidized bed is not persuasive.

Applicants argue that Flickinger does not disclose extracorporeal adsorption for removing harmful substances responsible of inducing sepsis caused by Gram-negative or Gram-positive bacteria, as claimed. In response to applicant's arguments against the Flickinger reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In this case, Jaber et al., teach extracorporeal adsorption method for treating gram-negative bacterial sepsis. Therefore, this argument is not persuasive since the references used within the instant rejections, teach extracorporeal adsorption for removing harmful substances responsible of inducing sepsis caused by Gram-negative or Gram-positive bacteria.

Applicants set forth that Jaber states on page 53 that to date, however, no treatment has been able to show consistent and reproducible benefit in clinical trials. However the entire paragraph refers to the pathogenesis of human sepsis and the annihilation of bacterial products, there is no statement within the Jaber et al., article

stating that extracorporeal adsorption for removing harmful substances responsible of inducing sepsis caused by Gram-negative or Gram-positive bacteria is not effective. Furthermore, it is noted that therapeutic utility sufficiency under the patent law is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs to marketed in the United States. Therefore, FDA approval from 1997 is not the basis of patentability. Thus, applicants' argument is not persuasive.

Conclusion

7. No claims allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/

Primary Examiner, Art Unit 1645